## Generation of pluripotent stem cell-derived mouse kidneys in Sall1-targeted anephric rats.

**Journal:** Nat Commun

**Publication Year:** 2019

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**PubMed link:** 30723213

**Funding Grants:** Generation of functional cells and organs from iPSCs

**Public Summary:**
We have previously shown that an approach called interspecies blastocyst complementation can be used to grow whole organs from pluripotent stem cells (PSCs) in an animal. The goal of this research is to alleviate the chronic shortage in donor organs for transplantation in cases of end-stage organ failure. Here, we demonstrate that this approach can be used to generate functional kidneys by growing mouse-PSC-derived kidneys in a rat. These studies provide proof-of-concept for generating human kidneys in animals, and a roadmap towards providing a reliable source of high-quality human kidneys for transplantation medicine.

**Scientific Abstract:**
Regeneration of human kidneys in animal models would help combat the severe shortage of donors in transplantation therapy. Previously, we demonstrated by interspecific blastocyst complementation between mouse and rats, generation of pluripotent stem cell (PSC)-derived functional pancreas, in apancreatic Pdx1 mutant mice. We, however, were unable to obtain rat PSC-derived kidneys in anephric Sall1 mutant mice, likely due to the poor contribution of rat PSCs to the mouse metanephric mesenchyme, a nephron progenitor. Here, conversely, we show that mouse PSCs can efficiently differentiate into the metanephric mesenchyme in rat, allowing the generation of mouse PSC-derived kidney in anephric Sall1 mutant rat. Glomerular epithelium and renal tubules in the kidneys are entirely composed of mouse PSC-derived cells expressing key functional markers. Importantly, the ureter-bladder junction is normally formed. These data provide proof-of-principle for interspecific blastocyst complementation as a viable approach for kidney generation.